UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,673	01/10/2001	James M. Wilson	GNVPN.019B1USA	8771

270 7590 02/22/2006

HOWSON AND HOWSON
ONE SPRING HOUSE CORPORATION CENTER
BOX 457
321 NORRISTOWN ROAD
SPRING HOUSE, PA 19477

EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/757,673	WILSON ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/30/06, 12/14/05, 10/19/05*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-10, 18-23, 25-27, 30-33, 36 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-10, 18-23, 25-27, 30-33, 36, 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Final Rejection

Claims 7-10, 18-23, 25-27, 30-33, and 36-37 are pending.

Applicant's traversal, the amendment to claims 7, 18, 25, 27, 30, 32, and 33, the amendment to the specification, the cancellation of claims 34-35, and the addition of claims 36-37 in paper filed on 10/19/05 and 12/14/05 is acknowledged and considered by the examiner.

The amendment filed on 1/30/06 to correct status of claims 30 and 33 is acknowledged by the examiner.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 120 to US application 08/708,188 filed on 9/6/96 (now US Patent 5,866,552) is acknowledged. However, the application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 25-27 of this application.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Claims 25-27: US application 08/708,188 does not recite the term "helper-free rAAV". US application '188 does not provide written support under 112 first paragraph for claims 25-27.

Therefore, claims 25-27 only have priority to PCT/US97/15692 filed on 9/4/97 for rAAV free of wild type AAV and adenovirus using adenovirus as the helper virus.

Applicant's arguments filed 10/19/05 have been fully considered but they are not persuasive.

In response to applicant's argument that on page 7, lines 13-24 of '188 there is written support for the term "helper-free", the argument is not found persuasive because '188 only provides support for rAAV which is substantially free of contamination with adenovirus or wild-type AAV. The definition of the term recited in the instant claims does not limit to the disclosure set forth on page 7. The term could read on using other viruses (e.g., herpes virus, vaccinia virus, aav, etc.) not supported by the disclosure of '188 to produce the AAV. See *Lockwood v. American Airlines Inc.*, 41 USPQ2d 1961, 1966 (CAFC 1997).

In response to applicant's argument that the precise words of the claim is not a requirement for written description where the meaning of the words is clear from the specification, the argument is not found persuasive because while it is acknowledged that the precise words are not a requirement for written description, the meaning of the words is not clear because the meaning of the word could be broader than the support provided in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-10, 18-23, 25-27, 30, 31, 32, 36, and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Matter Rejection:

The limitation 'produced using a helper virus' in amended claims 7, 18, 25, 30, 32, 36 and 37 (and claims dependent therefrom) is not supported by the instant specification. There does not appear to be a written description of the claim limitation 'produced using a helper virus' in the application as filed. See MPEP § 2163.06. Applicants cite several pages for support of the limitation, however the pages cited by applicant are directed to producing rAAV using adenoviral helper virus. The limitation is broader than the support provided in the specification. The helper virus could read on other viruses not supported the instant specification.

The limitation 'wherein the rAAV has been produced using a helper virus and purified such that the rAAV is free of contamination with immunogenic adenoviral helper and wherein the transgene is expressed in the cell in the absence of a destructive immune response to the rAAV-transduced' in amended claim 32 is not supported by the instant specification. There does not appear to be a written description of the claim limitation in the application as filed. See MPEP § 2163.06. Applicants do not cite support for the limitation and the examiner thoroughly search the specification, but could not find support the limitation.

The limitation 'wherein the rAAV was purified from helper virus such that a cytotoxic immune response directed against rAAV-transduced cells of the mammal expressing the protein

is not detected in the mammal' in amended claim 18 and claims dependent therefrom is not supported by the instant specification. There does not appear to be a written description of the claim limitation in the application as filed. See MPEP § 2163.06. Applicants cite page 15 and page 29 for support of the limitation. However, page 15 is directed to producing rAAV free of adenovirus or wild-type AAV. Page 29 is directed to an immunological response to adenovirus and not AAV because the adenovirus infects antigen-presenting cells. Neither page 15 nor page 19 is directed to producing rAAV such that a cytotoxic immune response is directed to rAAV-transduced cells of the mammal.

Applicant's arguments filed 10/19/05 have been fully considered but they are not persuasive.

Applicant argues that page 29, lines 10-13 provide support for claims 32 and 33 because while the example illustrates this with a vector carrying lacZ, this does not obviate the more general nature of the first paragraph of Example 5.

Applicant's argument is found persuasive and the rejection for claims 32 and 33 is withdrawn because the general nature of the claimed invention is directed to not generating an immune response to the helper virus, wherein the helper virus is an adenovirus. In addition, Applicant's arguments, see page 11, filed 10/19/05, with respect to the rejection(s) of claim(s) 7-10 and 12-24 under written description for the limitation "at least as free of adenoviral helper virus as is obtained..." have been fully considered and are persuasive. Therefore, the rejection has been withdrawn because of the amendment to the claims and cancellation of claims 12-17, 24, and 32-33. However, upon further consideration, a new ground(s) of rejection is made in

view of the amendment to claims 7, 18, 25, 30, 32 and claims dependent therefrom and the addition of new claims 36 and 37.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7-10, 18-23, 25-27, and 30-33 remain and claims 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Podsakoff et al (AI) taken with Colosi (US 6,004,797).

Podsakoff et al. teach a rAAV for gene therapy wherein the gene encoding human erythropoietin is under the control of the CMV immediate early promoter, has SV40 polyadenylation sequences at the 3' end, and these sequences are flanked by 5' and 3' AAV ITRs (columns 9-10, 16-17, and 21-22). Podsakoff et al. also teach that RSV promoter and other promoters can also be used for driving the expression of the gene of interest (columns 10-11). They also discuss the drawbacks of using adenoviral vectors for gene therapy, such as the elicitation of immune response to viral proteins, which would preclude subsequent treatments (column 1). Podsakoff et al. teach to purify the rAAV preparation by cesium chloride (CsCl) gradient centrifugation (column 14). Podsakoff et al. also teach to inject the rAAV vector in mice intramuscularly in heart and cardiac muscles (columns 19-20) and that erythropoietin is secreted by the myotubes or myoblasts (columns 4, 9-10 and 21-22). Podsakoff further teaches that human EPO gene was used as an example and that other suitable DNA sequences could be used that encode for proteins used for the treatment of different diseases (column 10). However, Podsakoff et al does not specifically teach an rAAV vector composition comprising 5' ITR, nucleic acid sequence encoding a secretable protein, and 3'ITR, wherein the level of contaminating helper virus (e.g., adenovirus) is no greater than that obtained by subjecting said recombinant rAAV to at least four rounds of cesium chloride centrifugation.

However, at the time the invention was made, Colosi teaches the problems associated with producing rAAV using helper virus or purifying the rAAV using a cesium chloride gradient (columns 2-3). Colosi teaches a method of producing rAAV comprising a heterologous nucleic,

wherein the rAAV is free of helper virus (e.g. adenovirus) (columns 5 and 8). Colosi further teaches that rAAV can comprise a transgene operably linked to a promoter (columns 2 and 10-11). Thus, one of ordinary skill in the art would reasonably determine that Colosi teaches a helper free rAAV or rAAV that is at least free of adenoviral helper virus as obtained by subjecting said rAAV to at least four rounds of cesium chloride because Colosi does not use replicant/functional adenovirus to produce rAAV.

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to combine the teaching of Podsakoff and Colosi to produce a composition comprising rAAV and a carrier, wherein said rAAV comprises 5' AAV ITR, nucleic acid encoding human apoE operably linked to a promoter and a 3" AAV ITR, wherein the rAAV is at least free of helper virus by subjecting the rAAV to CsCl gradient centrifugation. One of ordinary skill in the art would have been motivated to use the method of producing rAAV that is free of helper virus taught by Colosi instead of the method of producing rAAV taught by Podsakoff because Colosi teaches overcoming the problems of producing rAAV with a helper virus or the problems of using a CsCl gradient to purify the rAAV and producing a titer of rAAV that is equivalent or greater than using a helper virus to produce the rAAV (column 9).

In addition, at the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to combine the teaching of Podsakoff and Colosi to use a composition comprising rAAV and a carrier, wherein said rAAV comprises 5' AAV ITR, nucleic acid encoding human apoE operably linked to a promoter and a 3" AAV ITR, wherein the rAAV is at least free of helper virus by subjecting the rAAV to CsCl gradient centrifugation in a method of expressing a human apoE in a mammal by way of intramuscularly administering. One of

ordinary skill in the art would have been motivated to use the rAAV in the method because the immune response in the mammal to the rAAV would be reduced because of the absence of adenovirus, which is a problem associated with gene therapy as exemplified by Podsakoff (column 1). In addition, regarding the limitations in instant claims 25, 32, 33, and 35-36 and claims dependent therefrom, one of ordinary skill in the art would have reasonably expected that using the rAAV taught by Colosi in the method taught by Podsakoff would result in an absence of an antibody response/inflammation response/cytotoxic immune response against contaminating adenoviral antigens because Colosi did not use a replication competent/functional adenovirus to produce the rAAV.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 10/19/05 have been fully considered but they are not persuasive.

Applicant argues that the combined teaching fails to teach or suggest use of such a rAAV prepared using a helper virus and purified therefrom in the absence of a cytotoxic immune response to helper virus, immune response to helper virus is absent, in the absence of a destructive immune response to the rAAV-transduced cell, and in the absence of inflammation caused by contaminating helper adenovirus.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., therefrom in the absence of a cytotoxic immune response to helper virus, immune response to helper virus is absent, in the absence of a destructive immune response to the rAAV-transduced cell, and in the

absence of inflammation caused by contaminating helper adenovirus) are not recited in all of the rejected claim(s) (claims 7-10, 25-27, and 30-31). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, the specific conditions for using four rounds of cesium chloride gradient used by applicants (page 34) are not recited in the claims, any cesium chloride gradient is embraced by the claimed method. Thus, the claimed methods could read on any percentage of contamination with a helper virus.

In addition, the limitation "using a helper virus" does not have patentable weight over the prior because the limitation does not distinguished the claimed rAAV over the rAAV taught in the prior art.

In response to applicant's argument regarding the limitations in instant claims 25, 32, 33, and 35-36 and claims dependent therefrom, one of ordinary skill in the art would have reasonably expected that using the rAAV taught by Colosi in the method taught by Podsakoff would result in an absence of an antibody response/inflammation response/cytotoxic immune response against contaminating adenoviral antigens because Colosi did not use a replication competent/functional adenovirus to produce the rAAV.

Claims 7-10 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Podsakoff taken with Colosi as applied to claims 7-10, 18-23, 25-27, 30-33 and claims 36-37 above, in further of view of Fang et al 1995 (CS) and Kay et al (US 5,980, 886).

However, Podsakoff et al. taken with Colosi do not specifically teach rAAV comprising transgenes encoding factor IX, beta-interferon, insulin, erythropoietin, growth hormone, and parathyroid hormone.

However, at the time the invention was made, Fang et al teach gene therapy of hemophilia B using adenovirus mediated factor IX expression (see the abstract). They also teach that adenovirus mediated gene transfer in vivo results in only transient gene expression due to the destruction of adenovirally transduced cells by the host immune system (see first para of the introduction section). Fang et al also teach an adenoviral vector that contains the cDNA encoding factor IX protein (materials and methods section on page 1040).

At the time of the invention, it would have been prima facie obvious to one of ordinary skill in the art to modify the rAAV vector of Podsakoff et al. taken with Colosi by cloning the factor IX cDNA in it and use the resultant vector in gene therapy of hemophilia by injecting with reasonable success because the methods of making rAAV vector and gene delivery in muscles are taught by Podsakoff while Fang et al. teach a factor IX vector from which the factor IX cDNA sequences can be spliced out. One of ordinary skill in the art would have been motivated to use an adeno-associated viral vector in place of adenoviral vector because Fang et al. teach that adenoviral vector mediated gene delivery results only in transient gene expression due to immune response and therefore, an one of ordinary skill in the art would have used an alternative method of gene therapy to increase the length of gene expression.

Regarding the other proteins recited in instant claims 9 and 26, it is noted that at the time the invention was made, the cDNAs encoding the recited proteins were known to one of ordinary skill in the art and were subject of preparing vectors for expression of these proteins. For

example, Kay et al (US 5,980, 886) taught a vector for expression of proteins in liver and they listed insulin, growth hormone, erythropoietin, ApoE, parathyroid hormone, interferons, and several other proteins that could be expressed using their vector system (column 3). Therefore, one of ordinary skill in the art would have been enabled to make recombinant AAV expressing recited proteins, such as insulin, growth hormone, erythropoietin, ApoE, parathyroid hormone, interferons, at the time of the claimed invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to make such vectors because all these proteins were known to be associated with a disease therefore, making such vectors would have helped in devising and developing therapeutic strategies.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 10/19/05 have been fully considered but they are not persuasive because the applicants are based on arguments that were already not found persuasive for the reasons set forth under the previous 103(a) rejection.

Claims 25, 26, and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chiorini (AAB) taken with Dwarki et al. (US 6,221,646). Chiorini teaches intramuscularly delivering a composition comprising AAV comprising a nucleotide sequence and a carrier (column 3). Chiorini teaches that the nucleotide sequence can encode Factor IX, insulin, and apoE (column 3). However, Chiorini does not specifically teach using helper free rAAV in the method, such that an immune response to the helper virus generated by administration of rAAV

is not detected upon administration of the rAAV. In addition, Chiorini does not specifically teach using a nucleotide sequence encoding growth hormone in the method.

Dwarki et al. (US 6,221,646) can be used in a prior art rejection against the instant claims 25 and 26 for the reasons set forth under priority.

However, at the time the invention was made, Dwarki teaches that a simple and efficient method is needed for producing rAAV. Dwarki teaches the production of rAAV substantially free of helper virus suitable for gene therapy and teaches a method for delivering to host cells a composition comprising a replication-defective recombinant AAV virions substantially free of wild-type AAV and helper adenovirus, wherein the virions comprise a nucleotide sequence (columns 1 and 14). Dwarki further teaches that the nucleotide sequence can encode Factor IX, insulin, and growth hormone (columns 4 and 9). However, Dwarki does not specifically teach intramuscularly delivering a composition comprising AAV and a carrier to a mammal.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Chiorini taken with Dwarki, namely to use rAAV substantially free of helper virus in a method of intramuscularly administering a composition comprising rAAV comprising a nucleotide sequence. One of ordinary skill in the art would have been motivated to use rAAV substantially free of helper virus taught by Dwarki in the method because Dwarki teaches that the helper free rAAV are suitable for gene therapy and can be produced using a simple and efficient method. In addition, one of ordinary skill in the art would have been motivated to combine the references to intramuscularly administer said composition comprising rAAV and a carrier to a mammal because Chiorini teaches that

intramuscularly a composition comprising AAV is a routine delivery route for one of ordinary skill of the art for delivering AAV to a mammal.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Chiorini taken with Dwarki, namely to deliver a nucleotide encoding Factor IX, apoE, beta interferon, insulin, or growth hormone to the mammal using the method. One of ordinary skill in the art would have been motivated, as a matter of design choice, to combine the references to use a nucleotide encoding a secretable protein in the method, wherein the protein is selected from Factor IX, apoE, beta interferon, insulin, and growth hormone because these proteins were well known to one of ordinary skill in the art for use in a method of delivering a transgene to a mammal using an rAAV.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 10/19/05 have been fully considered but they are not persuasive.

In response to applicant's argument that the claims clarify over the prior art that the method utilizes rAAV prepared using a helper virus and purified therefrom, the argument is not found persuasive because the limitation "rAAV produced using a helper virus and purified of helper virus" does not have patentable weight over the prior art because the rAAV is not structurally different than the rAAV taught by Chiorini taken with Dwarki.

In response to applicant's argument that the applicants believe Dwarki is not available as prior art, the argument is not found persuasive because Dwarki uses a different method to

produce the rAAV free of wild type AAV and adenovirus (which is not disclosed in the earliest priority date).

In response to applicant's argument that Chiorini and Dwarki fail to teach or suggest use of such a composition or the purification of rAAV such that an immune response to helper virus is absent upon administration of the helper-free rAAV, the argument is not found persuasive because the limitation does not have patentable weight over the prior art. The product taught by the prior art is the same product as recited in the instant claims. Thus, it would have been obvious to one of ordinary skill in the art that an immune response to the adenovirus generated by administration of rAAV is not detected upon administration of the rAAV taught by Chiorini and Dwarki.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 7-10, 18-23, 25-27, and 30-33 remain and claims 36-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

claims 1-4 of U.S. Patent No. 5,866,552 for reasons of record set forth in the previous office action of 11-23-01.

Applicants' request that this rejection be deferred until allowance is acknowledged.

Response to Arguments

Applicant's arguments, see pages 10-11, filed 10/19/05, with respect to new matter have been fully considered and are partially persuasive. Upon further consideration of the specification, the rejection of the limitation in claim 27 has been withdrawn because the specification provides written description for the claim. See page 35. Inserting any gene into the AAV would not change the limitation.

Applicant's arguments, see page 13, filed 10/19/05, with respect to enablement rejection have been fully considered and are persuasive. The rejection of claims 32-35 has been withdrawn because of the cancellation of claims 34 and 35 and the amendment to claims 32 and 33 to recite intramuscularly administration to skeletal muscle.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE – Art Unit 1635, can be reached at (571) 272-0811.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian D Whiteman